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# Insights on Microemulgel as a Topical Drug Delivery System

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**A B S T R A C T**

Microemulgels have become a potential topical drug delivery method because they combine the advantages of hydrogels and microemulsions. This paper aims to provide a broad review of microemulgels as an effective and versatile topical pharmaceutical delivery technology. Transparent, isotropic, and thermodynamically stable systems are microemulgels. comprising water, oil, surfactant, co-surfactant, and a gelling agent. They possess unique properties such as increased stability, regulated release, improved penetration, and better solubility of medications. Because of these characteristics, microemulgels can be used to deliver a variety of therapeutic agents, such as hydrophilic and hydrophobic drugs, proteins, and peptides. Combining hydrogels and microemulsions in microemulgels has several advantages. Although hydrogels offer viscosity, ease of implementation, and sustained drug release, microemulsions offer high drug loading capacity, fast drug release, and enhanced skin penetration. The combination of these two systems in a microemulgel produces a synergistic effect that improves therapeutic results and drug delivery efficiency. Microemulgel formulation has been done using a variety of methods, such as phase inversion temperature, spontaneous emulsification, and self-emulsification. Numerous studies have been conducted on the variables that affect the gel's stability and performance, including the concentration of the gelling agent, the ratio of oil to water, and the choice of surfactant or co-surfactant. Additionally, microemulgels provide a range of administration routes, such as ophthalmic, transdermal, and topical. They can be customised to have the appropriate rheological qualities, which will make application simple and patient compliance high. In summary, microemulgels are a potentially useful method of delivering drugs via the skin. They are an important tool in the pharmaceutical and cosmetic sectors because of their special qualities, adaptability, and capacity to encapsulate a variety of medicinal substances. To fully realize their potential, improve formulations, and assess their safety and effectiveness in clinical settings, more research is required.

Keywords: Microemulsion, Microemulgel, Topical drug delivery, Hydrophobic drug, gel,

## 1. Introduction

In 1940, Hoar and Schulman initially proposed the idea of micro-emulsion.[1] The purpose of this paper is to give a general overview of microemulgels as a productive and adaptable delivery system for medications through the skin. Microemulgels consist of water, oil, surfactant, and co-surfactant, together with a gelling agent. They are clear, thermodynamically stable, and isotropic systems. They have special qualities like better medication solubility, better penetration, regulated release, and more stability. These properties make microemulgels suitable for the delivery of a wide range of therapeutic agents, including hydrophilic and hydrophobic medicines, proteins, and peptides. There are various benefits to using hydrogels and microemulsions together in microemulgels. [2]

The goal of topical distribution is to prevent the metabolic breakdown and gastrointestinal incompatibilities that come with oral treatment. Furthermore, topical administration offers enhanced bioavailability and stable drug delivery at prolonged release rates from topical dose forms based on the physicochemical characteristics of the drug and the carrier. Water, oil, and amphiphilic, a thermodynamically stable and optically isotropic liquid micro-dispersion, are the constituents of microemulsion. Many medications' distribution, effectiveness, and bioavailability are enhanced via micro-emulsion. A "microemulsion" is a transparent, thermodynamically stable dispersion of two immiscible liquids, such as water and oil, that is maintained by surfactant molecules through the formation of an interfacial film. A microemulsion is defined as a liquid dispersion of an aqueous phase and a lipid phase with a surfactant that is kinetically stable. The dispersed particles have a small oil/water interfacial surface tension and range in size from 5 to 200 nm. [3] Topical preparation lowers GI discomfort, stops the medicine from being metabolized in the liver, and increases the drug's bioavailability. Topical medications act immediately at the location of the action. [4]

### *1.1 Anatomy and physiology of skin:*

The skin on an adult average has a surface area of around 2 m^2 and receives approximately 1/3 of the blood that circulates through the body. Per square meter of skin, the normal human has between forty and seventy hair follicles and between two and three hundred sweat ducts. Skin has a pH range of 4 to 5.6. The pH of skin is influenced by fatty acids released from sebum and sweat. The skin is made up of four different tissue layers: the subcutaneous connective tissues, viable dermis, viable epidermis, and non-viable epidermis. [5,6]

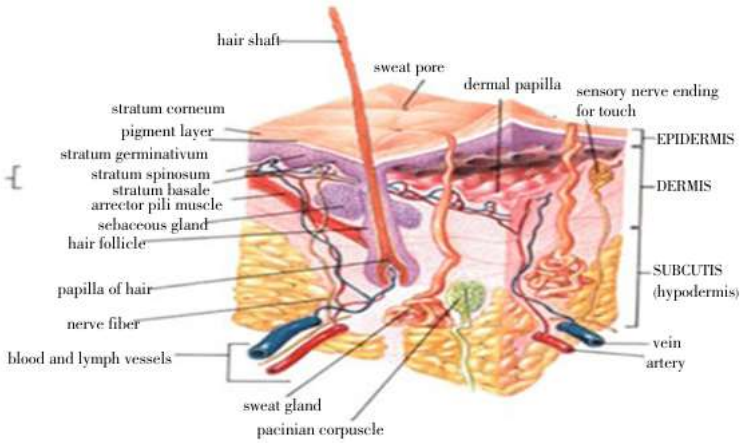


Figure. 1 Anatomy of Skin [7]

### *1.2 Topical drug delivery system*

Topical drug delivery products fall into two main categories: internal and exterior topicals. The internal topicals are given to the mucosal membrane orally, vaginally, or on the rectal tissues for local activity, while the exterior topicals are distributed, sprayed, or otherwise dispersed on the tissue to cover the diseased area. Topical drug delivery systems have several advantages, including the ability to avoid first pass metabolism, prevent gastrointestinal incompatibilities, target specific sites, improve patient compliance, enable simple and convenient self-medication, and allow for the easy termination of medication when needed. [8] Topical drug delivery systems have a number of drawbacks, including the potential for allergic reactions, poor drug permeability through skin, difficulty absorbing medications with large particle sizes through skin, and skin irritation from contact dermatitis. Skin has a complicated structure and is thick. Moving from the environment, molecules must pass through the stratum corneum and any surface-deposited endogenous or foreign substances. Then, in order for them to be eliminated from the skin by blood or lymph flow, they must penetrate the viable epidermis, the papillary dermis, and the capillary walls into the blood stream or lymph channels. It is evident that moving across the skin membrane is a complicated process and analytical difficulty. The physio-chemical and physical factors that affect the topical drug delivery system include molecular weight, partition coefficient, degree of ionization, effect of vehicle, and thickness, hydration, pH, and inflammation of the skin, as well as lipid content, densities of hair follicles and sweat glands, blood flow, and so on. [9]

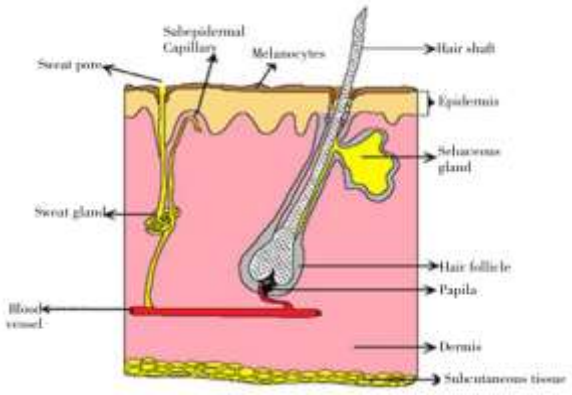


Figure 2. Various routes of penetration of drugs through skin. [10]

## 2 Benefits of Drug Delivery Systems for Topical Use:[11]

Compared to other transdermal formulations, microemulgels have the following benefits:

- Higher loading capacity
- More affordable and feasible production
- Hydrophobic drug incorporation
- Controlled release
- No intense sonication

- Enhanced absorption and bioavailability
- Defense against hydrolysis and oxidation
- Non-greasy and easy to wash off
- Improved patient compliance
- And equivalent dose reduction when compared to oral administration.

## 3 Drawbacks of micro-emulsion based gel: [12]

- Drugs with larger particle sizes have trouble being absorbed through the skin.
- Transdermal permeability is low in certain drugs.
- Drugs with very low bloodstream concentrations that exert their effects are appropriate for transdermal administration.
- The possibility of allergic responses exists. The drugs may be broken down by enzymes found in the skin.

## 4. Component of microemulsion based gel [13]

### *4.1 Oil phase:*

The kind of oil selected depends on the medication and the mode of administration. The screening oil ought to be able to completely soak the drug. The oil can increase its surfactant tail group and affect its curvature. Some properties of saturated and unsaturated fatty acids facilitate penetration. Another unsaturated fatty acid that significantly improves skin penetration is oleic acid. Since semi-synthetic oils are more stable than natural oils, their use has grown recently. To effectively establish an o/w microemulsion system, medicines that are poorly soluble in water must be soluble in the dispersed oil phase. Even as oil concentration grows, the o/w microemulsion causes droplet size to increase. [14]

### *4.2 Aqueous phase:*

Preservatives and hydrophilic active components may be present in the aqueous phase. The most prevalent substance in watery phases is water. [15]

### *4.3 Surfactants:*

Low-level reduction of interfacial tension is the primary function of surfactants. This will facilitate the dispersion of the microemulsion and result in a flexible film with the proper lipophilic properties to provide the proper curvature at the interfacial region. It can also easily diverge from surrounding droplets. The following are examples of surfactants that stabilize microemulsion systems. Some examples of surfactants for stabalize microemulsion system:

- Non-ionic,
- Zwitterionic,
- Cationic,or
- Anionic

The interactions between the aqueous phase and the surfactant's hydrophilic finish affect a microemulsion's stability, Depending on whether the surfactant is ionic or non-ionic, these interactions change. Non-ionic surfactants rely on hydrogen bond and dipole interactions with the water's hydration layer on their hydrophilic surface, whereas ionic surfactants are further made accessible through the electrical double layer. As such, ionic surfactants have a greater effect on the stability of an emulsion or microemulsion than non-ionic surfactants. However, ionic surfactants are typically not advised for use in pharmaceutical applications due to toxicity concerns. Non-ionic surfactants are commonly believed to be well-suited for use in pharmaceutical formulations. As per conventional knowledge, the production of water-in-oil (w/o) and oil-in-water (o/w) microemulsions should be accomplished with low HLB (3-6) and high HLB (8-18) surfactants, respectively. Co-surfactants are sometimes required to lower the advantageous HLB of surfactants with a value above 20 in order to achieve the ideal range for microemulsion production. [16]

### *4.4 Co-surfactants:*

Single-chain surfactants can't produce microemulsions on their own because of their limited ability to lower the interfacial tension between water and oil. Co-surfactants are employed to get around this restriction and improve the flexibility of the interfacial film, enabling the creation of microemulsions with a range of compositions. The lipophilic chains of the surfactant must be sufficiently brief or contain fluidizing groups, such as unsaturated bonds, when

using a single surfactant film. Co-surfactants, such as alcohols with short to medium chain lengths (C3–C8), are widely employed to improve the fluidity of the interface and further reduce the interfacial tension. [17]

## 5. Formulation

### *5.1 Procedures for Formulating Microemulgel :*

There are three steps used to induce microemulgel [18].

Step 1. Using oil painting phase and water phase, prepare an oil painting in water or water in oil painting microemulsion.

Step 2. Making gel with water and a gelatinizing agent while continuously stirring and conforming pH.

Step 3. To produce microemulgel, incorporate the microemulsion into the gel foundation [19, 20].

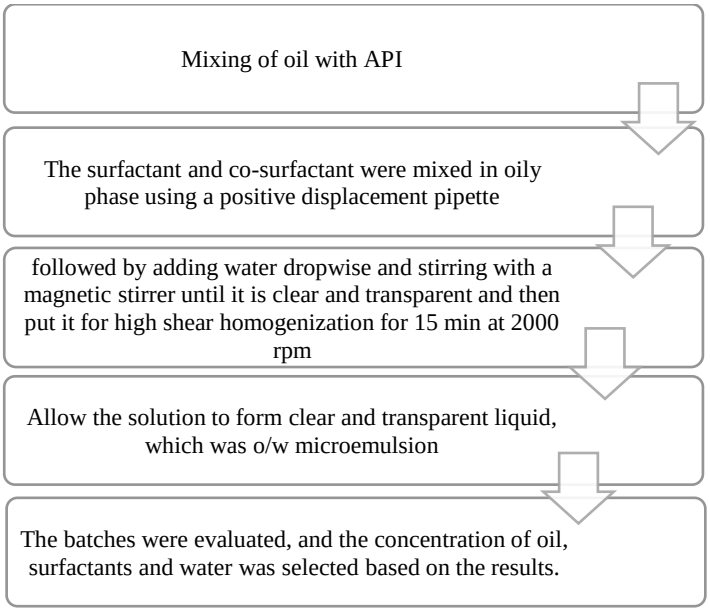


Figure 3. Formulation of Microemulsion

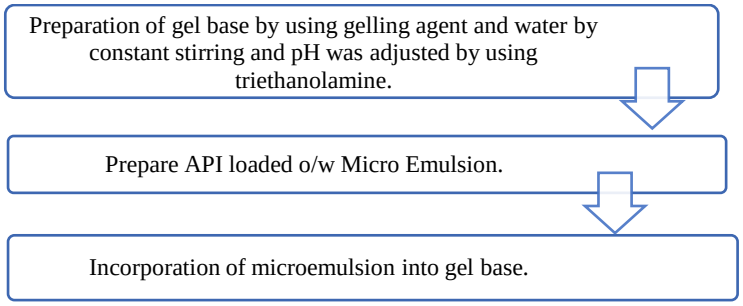


Figure 4. Formulation of Microemulgel

High intensity emulsification fashion use homogenizers and ultrasonicators to strongly smash through the innards and introduce nanosized driblets. To stabilize the expression in this approach, external energy is demanded. [21]

Low energy emulsification fashion While creating a microemulsion, low energy ways are preferable to high energy tactics. The robotic fashion and the phase inversion fashion are exemplifications of low energy ways. The phase inversion approach calls for blending wetting down agent, water, and oil painting in a largely specified rate. A nonstop phase of nanoscale drops product results from the titration of the oil painting phase with the waterless phase while stirring continuously. The addition of wetting down agent & co-surfactant affects the emulsification system.

The quantum of wetting down agent used in the expression determined which kind of conflation is formed the temperature plays an important part in the conformation of conflation. At low temperatures, they're hydrophilic and oil painting in water type. They're water- in- oil painting type and lipophilic at advanced temperatures. At associate degree intermediate temperature, microemulsion. happens with the waterless phase & oil painting part to make a bicontinuous structure.

For the unstable element, the robotic fashion is specifically employed; else, a temperature-dependent robotic twist ofnon-ionic wetter is used for exertion during the part inversion fashion. The mixes fashioned at part inversion temperature are going to be reversed on cooling with nonstop shifting.

This system is also confined to include the unstable element, though limitation takes as approach reduced part inversion temperature by applicable choosing surfactant [22].

## 6. The microemulsion evaluation [23]

1. viscosity: viscosity is measured with a Brookfield Rotational Viscometer.
2. pH: A digital pH metre can be used to measure pH.
3. Drug Content: Using the proper solvent, API is extracted from a microemulsion based on API. A UV-visible spectroscopy technique is used to quantify the concentration at its maximum wavelength utilizing solvent as a reagent blank.
4. Centrifugation: This is evaluated in order to determine whether the physical system is stable. To check for creaming or phase separation in the system, a microemulsion is centrifuged at room temperature for 10 minutes at 5000 RPM. We'll evaluate the visual appeal of the system.
5. Conductivity: A digital conductometer is used to assess the microemulsion's electric conductivity at room temperature. [24]
6. Dilution Test: If a continuous phase is present, the microemulsion will not be split into stages. A 50–100 times continuous phase dilution will be followed by a visual evaluation of the microemulsion's purity and phase separation.
7. % Transmittance Measurement: In the continuous phase, the micro-emulsion will be diluted 50–100 times. A UV-Visible spectrophotometer is used to measure the transmittance of the formulation at a certain wavelength.
8. Zeta potential and Micelle Size Analysis: A particle size analyzer is used to calculate the microemulsion's zeta potential, size distribution, and micelle size.
9. In vitro release investigation: Franz diffusion cells are employed in this investigation.

### *6.1 Characterization of Microemulsion-Based Gel [25]*

1. Physical Inspections: The microemulsion-based gel's color, homogeneity, uniformity, and texture are examined physically.
2. pH: A digital pH monitor is used to measure the pH of the 1% aqueous solution used to make the microemulsion-based gels.
3. Spreadability Dimension: 0.5 g of a gel based on microemulsion is put inside a pre-marked, 1 cm-diameter circle and set on a glass plate. To test spreadability, a second plate is placed over the plate. The five grams of weight are allowed to rest on the upper glass plate for five minutes. The diameter increase of the microemulsion-based gel spreading is measured in cm/gm-sec.
4. Rheological study: The viscosity at 37°C is mostly measured using the Brookfield Viscometer.
5. Determining the drug content: Having a backup plan in place is a great idea, especially if you anticipate traveling frequently. A UV spectrophotometer is used to measure absorbance at maximum nm following an appropriate dilution.
6. Extrudability Test (Tube Test): A microemulsion-based gel formulation's extrudability can be evaluated by measuring the force required to extrude material from the tube.
7. In-vitro release study: This research makes use of Franz diffusion cells.
8. An examination into drug release kinetics: The results of each batch's in-vitro release profiles are shown as

Zero order kinetic models – percentage CPR vs time.

First order kinetic model – log % cumulative drug remaining Vs time.

Higuchi’s model – % cumulative drug released vs. square root of time.

Korsmeyer/Peppa’s model – log % cumulative drug released Vs log time.

Hixson Crowell model – Cube root of % drug to be remaining Vs Time.

Skin Irritation: It is done on a rabbit utilising the Draize-patch test.

In-vivo investigation: the study of animals. Gel based on microemulsions is optimised.

## 7. CONCLUSION:

The increased patient compliance in recent years has led to a widespread adoption of topical medicine delivery devices. Micromulgels have shown to be a particularly successful method of administering hydrophobic drugs among these systems, and they also show great promise for mixing drugs that are hydrophilic and hydrophobic. Microemulgels combine the benefits of emulsions and gels, microemulsions in one formulation to allow for the control of drug release rates for short half-lives. Even though there aren't many gel formulations based on microemulsions that are already on the market, there is a lot of room for growth and study in this field. Microemulgel improves drug moieties' deposition at the location, therapeutic action is likewise raised. Microemulgels have many advantages and show potential for a wide range of derma care uses in the future. They are beneficial because they have fewer too fatty bases and excipients, which improves the medication's effectiveness.

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